--**19. Cancelled:** A method of diagnosing cancer in a human subject by applying the method of claim 17 to a sample of the subject's peritoneal fluid, pleural fluid or bronchial washings.

Cancel Claim 20: in its entirety.

--**20. Cancelled:** A method of diagnosing cancer in a human subject by applying the method of claim 18 to a sample of the subject's peritoneal fluid, pleural fluid or bronchial washings.

REMARKS

1. In Paragraph 3 of the Office Action of October 22, 2002, the Examiner has objected to claim 19 and 20 under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 19 and 20 have now been cancelled.

2. In Paragraph 4 of the Office Action, the Examiner has rejected Claims 1-16 under 35 U.S.C. 103(a) as being unpatentable over Katopodis (US 5,045,453) in view of Gernez-Rieux et al (Pathologie et al Biologie, 1963, Vol. 11, pp. 729-741) on the ground that it would have been prima facia obvious to one of ordinary skill in the art to use the method of Katopodis for the determination of sialoprotein in sputum of patients having bronchitis and asthma, not cancer, as this is not a specific embodiment of

Claims 1-16."

Claim 1 has now been amended to limit the application of the method claimed in claim 1 to patients having cancer or suspected of having cancer. Applicant believes that this amendment overcomes the rejection of Paragraph 4.

3. In Paragraph 5 the Examiner maintains the previous rejection of claims 1-16 under 35 U.S.C. 103(a) as being unpatentable over ***Katopodis*** (U.S. 5,045,453) in view of ***Bellahcene et al*** (British Journal of Haematology, 2000, Vol. 111, pp. 1118-1121). The Examiner contends: a) that it would be obvious for one skilled in the art to optimize parameters such as centrifugation speed and the washing of a layer to separate a component of a mixture; and b) that the applicant has improperly attacked the references individually when the rejection is based on a combination of the references.

Applicant respectfully traverses this rejection.

a) ***Katopodis*** teaches a method of extracting sialoprotein from serum and plasma. It does not teach a method of extracting sialoprotein from cerebrospinal fluid, urine, saliva, sputum, peritoneal fluid, pleural fluid or bronchial washings.

b) The Examiner combines ***Katopodis*** with the teaching of ***Bellahcene et al.*** ***Bellahcene*** teaches the detection of multiple myeloma comprising the detection of sialoprotein in plasma cells of bone marrow. ***Katopodis*** teaches only the extraction of sialoprotein from blood plasma or serum.

c) ***Katopodis*** teaches a method in the chemical art. ***Bellahcene*** teaches in the totally different art of cell culture and cytology, not chemistry. There would be no reason whatsoever for a chemist to combine a teaching in cytology to aid in discovering the chemistry necessary to extract, isolate and measure the LSP complex as taught by the subject invention. In fact it is doubtful that one skilled in the chemical art would even understand a teaching in cytology, a completely different and unrelated art.

d) ***Katopodis and Bellahcene*** do no more than confirm applicant's observation that it has long been known that tumor cells cause changes in the metabolism of sialic acid. Specification, page 4, lines 17-20.

e) As with ***Katopodis and Bellahcene***, the tumor markers of the prior art deal principally with sialoprotein in whole blood, blood serum or plasma cells in bone marrow resulting from systemic tumors. None of the prior art references, either alone or in combination, teach a cancer diagnostic test for other body fluids such as CSF.

f) The invention takes a major step beyond these serologic markers of the prior art. It teaches that the cellular material or debris of the tumor, or of the surrounding cells in response to the tumor, is diffused into the body fluid, most notably the CSF. Specification, page 5, lines 6-10. It further teaches a method for determining the levels of LSP in CSF and other body fluids providing a reliable test for distinguishing a malignant brain tumor from a benign brain tumor and for monitoring a patient's response to treatment. Specification, page 6, lines 20-23.

g) Applicant concedes that there are other methods and procedures for

distinguishing malignant brain tumors from benign tumors. However, these methods require tissue samples, which is not practical on a routine basis particularly in the case of brain tumors. Specification, page 2, lines 9-19.

h) If , as in ***Bellahcene***, there are tissue samples of the tumors available, there is no need for the method of the invention. The importance of the invention is that it provides a reliable test in situations where there are no tissue samples easily available as in brain cancer, or when the development of the tumor is in such early stages that analysis of the tissue samples is not determinative. In these cases material from the cancer cells, which have diffused into the CSF, can be measured for levels of the LSP complex providing a reliable test for the presence of a malignant tumor.

In summary, the prior art references, in addition to being in different arts, deal with the analysis of blood, serum, or plasma cells from bone marrow, not of CSF or other body fluids. Moreover, the prior art markers such as ***Katopodis and Bellahcene*** require tissue samples. The method of the invention does not require tissue samples but is able to measure the LSP levels of cellular material produced by tumor cells, or cells in response to the tumor, which has been diffused into the body fluids such as CSF.

Applicant respectfully submits that the combination of ***Katopodis and Bellahcene*** do not render the invention obvious under 35 U.S.C. 103.

4. Applicant acknowledges that in Paragraphs 6 and 7 the Examiner has withdrawn previous rejections of claims 1-17 and claim 17 as being unpatentable under

35 U.S.C. 103(a).

5. In Paragraph 8 of the Office Action, the Examiner has rejected claims 1-20 under 35 U.S.C. 112, second paragraph, as being indefinite for failure to particularly point out and distinctly claim the subject matter of the invention. Specifically the claims are rejected because applicant amended claim 1 to read on "high" speed centrifugation, which the Examiner contends, has rendered the claims indefinite.

Applicant has now amended claim 1 subparagraph c to delete the reference to "high" speed centrifugation and to claim centrifugation "of about 6000 rpm." Applicant believes that this amendment of claim 1 overcomes the rejection under 35 U.S.C. 112.

CONCLUSION

Applicant submits that the subject application, as amended herein, is now ready for allowance.

Respectfully submitted,

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